the regression. The relation is highly significant and shows potential as a predictive tool, but we agree that further experience is necessary.

The standard deviation of error from the regression estimate is a valid and generally understood statistic. If we had been proposing this relation as a specific predictive tool then we would have defined several different confidence levels. The variation due to errors in estimating the regression parameters also would have been included. In our study, the 95 percent confidence limits would be ±29.0 mm Hg at the narrowest point, not the 28 mm Hg stated by Riggs and Hirschfeld. At the upper extreme range of the observations, 95 percent confidence limits of ±32.4 mm Hg reflect errors in the estimate of the parameter b = 298. This means that for an $\bar{h}/r$ ratio of 0.71 the estimate is 217.9 ± 32.4 mm Hg, or 95 percent confidence limits of 185.4 to 250.3. In spite of the amount of variation, we believe that such estimates are good enough to be very useful, although further refinements and additional observations may improve our estimate of the best predictive tool.

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PORCINE HETEROGRAFTS IN TRICUSPID POSITION

In their report on structural change in porcine heterografts, Spray and Roberts[1] described five stenotic and thrombosed bioprosthetic valves. Although tricuspid valve replacement accounted for 29 percent of replaced valves, thrombotic stenosis of bioprostheses in the tricuspid position accounted for 40 percent of all thrombosed and stenotic valves. Fishbein et al.[2] reported on one patient in their series who underwent tricuspid valve replacement and who died 5 days postoperatively in a low output state. No anatomic cause was found to explain this patient's death. This relatively large incidence of thrombotic and low output complications associated with the stent mounted porcine heterograft in the tricuspid position should not be surprising because the valve is, most likely, structurally unsuitable for the low pressure right-sided atrioventricular position. While evaluating the echocardiographic appearance of this valve,[3] we found that the valve leaflets did not open fully when exposed to lower levels of flow. With decreasing flow past the valve, there was decreasing leaflet movement. At a very low stroke volume, the posterior muscular leaflet did not move at all.

Thrombosis about the tricuspid position bioprosthesis may have been induced by stasis of blood around the valve caused by incomplete valve opening and a low cardiac output. The porcine aortic tissue evolved over a million years to be opened rapidly by a high pressure ventricle. A grossly dilated and fibrillating right atrium, which is present in most patients with advanced tricuspid valve disease, may not generate a sufficient rate of rise of pressure to open this bioprosthesis adequately.

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3. **Horowitz MS, Tecklenberg PL, Goodman DG, et al:** Echocardiographic evaluation of the stent mounted aortic bioprosthetic valve in the mitral position. In vivo and in vitro studies. Circulation 54:91–96, 1976

REPLY

Horowitz may indeed be right in his contention that there is a relatively large incidence of thrombotic complications associated with stent mounted porcine heterografts in the tricuspid position and that these substitute cardiac valves may not be suitable for the low pressure of the the right-sided atrioventricular valve position. He may indeed be right, but I think there is not enough information to make that judgment at the moment. We simply reported the observations made in the necropsy patients we have studied. From our study it would not be possible to come to a conclusion regarding increased frequency of thrombus formation on the right-sided valve compared with the left-sided valve and certainly not the conclusion that this prosthesis is unsuitable for the tricuspid valve position.

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SUDDEN DEATH: HOW UNEXPECTED?

The case reported by Lawrence E. Hinkle et al.[1] was heralded as an example of "unexpected sudden death," yet throughout the report there is evidence of increasing hypertension, documented rhythm disturbances, anginal episodes (up to 10 daily) and, finally, symptoms compatible with early left ventricular failure. Certainly these symptoms and findings would lead the astute clinician to conclude that sudden death was a real probability.

Second, the report makes no mention of the patient's ever receiving adequate treatment for his hypertension, rhythm disturbances or angina pectoris. In fact, the only medication the patient was receiving was Coumadin,® 2.5 mg/day. Furthermore, there is no evidence that the patient had a thorough cardiac evaluation with echoelectrocardiography, and particularly coronary arteriography, to delineate whether he might have been helped with surgical myocardial revascularization. It is conceivable that these aspects of the patient's course were deleted from the case report; if not, the lack of diagnostic and therapeutic medical attention in this 61 year old man seems appalling.

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Reference

1. **Hinkle LE Jr, Argyros DC, Hayes JC, et al:** Pathogenesis of an unexpected sudden death: role of early cycle ventricular premature contractions. Am J Cardiol 39:873–879, 1977

REPLY

The subject of our report was invited to participate in our studies because his medical record at his employer's indicated that he was probably at high risk of sudden death. He and 332

similar men, employed in 19 industries, two labor unions and two public authorities in the New York metropolitan area, volunteered to take part in these studies. It was agreed that these men would continue under the care of their private physicians and that we would forward complete reports of our findings to their private physicians and (with their written permission) to their company physicians as well.

When this man was first examined in 1971, a letter describing in detail all of our findings and all our recommendations was sent to his physicians, and our examining physician discussed these with the participant himself in detail. At subsequent examinations, when there were significant new findings, these were also discussed with him and were communicated to his physicians.

The patient's role: The chief obstacle to the adequate treatment of this man was his own personality. He minimized his symptoms, sometimes denied their existence and concealed them from his associates. He disdained medication, preferred not to take nitroglycerin for his angina and would not change his routine of activities in any way. In 1973, in the interval between examinations, electrocardiographic evidence of a new myocardial infarction developed, but he denied having had any symptoms during this period and he lost no time from work. On many occasions he would not visit his physician regularly despite his physician's urging and our urging. At the time of his death he had not seen his physician for 3 months. The story of his increasing shortness of breath and probable congestive heart failure occurring in the weeks before he died was obtained more from his wife and friends than from him, and most of the information was obtained after his death.

Role of clinical findings: Other features of his case, in addition to his concealment of symptoms, tended to obscure the seriousness of his condition. His hypertension was manifested mostly during the day when he was active and challenged by his surroundings. When he was in his physician's office or at the company medical department his blood pressure was repeatedly recorded in the range of 130/80 mm Hg. The shadow of his heart on X-ray examination did not reflect the magnitude of his myocardial hypertrophy. The cardiothoracic ratio remained less than 50 percent. It was not until late in his course that roentgenologists began to describe his heart as "enlarged." The evidence of an electrocardiographic "pattern of left ventricular hypertrophy" was limited to an R wave of 15 mm in lead aVL. Echocardiography, which might have revealed the hypertrophy, was not available as a part of the original protocol in 1971. Thus, with the information available during much of his course, there was legitimate medical reason to question whether he required antihypertensive treatment.

To the casual medical observer, to whom this man minimized his symptoms, he appeared to be an active person with labile hypertension who had had two myocardial infarctions in the past but who was doing relatively well. As for his arrhythmias, his ventricular premature complexes were few (less than 1/1,000 complexes), asymptomatic and discernible only on tape recordings. The importance of early cycle ventricular premature complexes in the pathogenesis of sudden cardiac death outside the hospital was not appreciated until several years after his initial examination.

Prevention of sudden death: Regardless of these considerations, Mielke raises an important question with regard to unexpected sudden cardiac death. Our studies and the reports from Seattle and Miami all indicate that sudden cardiac death occurs only rarely in people without previously detectable heart disease. In the majority of cases it occurs in people with readily recognizable heart disease whose seriousness is not appreciated. Our experience also suggests to us that failure to control the hypertension, the congestive heart failure, the evidence of ischemia, the patterns of activity and probably the body weight and metabolic abnormalities of the patient may cause "unexpected sudden death" to occur sooner than it otherwise might. Thus it appears to us that although the primary control of "risk factors" for heart disease may lie within the realm of preventive medicine and public health, the immediate prevention or delay of sudden cardiac death must be the primary responsibility of physicians who are engaged in the long-term care of patients with heart disease.

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SEPTAL DEFECT IN TRANSPOSITION OF GREAT ARTERIES

Hazan et al.[1] state that their patient survived to age 9 years "in spite of the coexistence of a complete form of atrioventricular (A-V) canal." Although no one can deny the importance of the serious hemodynamic disturbances caused by A-V canal, it was precisely the presence of this large A-V defect that permitted their patient's survival and caused her to have only "slight cyanosis." Had there been no septal defects, the severity of the malformation would have been due to the fact that—in the authors' own words—"blood circulation is the same as in transposition of the great arteries," that is, a severe, poorly tolerated and deeply cyanotic condition. One must bear in mind that the artificial creation of a large atrial septal defect (atrial septostomy) salvages many infants with transposition of the great arteries, again precisely because it allows a bidirectional shunt across the newly created defect and it improves arterial oxygen saturation. The authors' patient already had a very large septal defect permitting a large and useful bidirectional shunt.

Hazan et al. discarded the term "isolated ventricular inversion in situs inversus" because ". . . in total situs inversus, ventricles are inverted by definition." Not so. In situs inversus all the heart chambers and all the viscerae are the mirror-image of normal and therefore *the ventricles are not inverted for this situs*. Yet, a given case of situs inversus, such as the authors' (and ours mentioned in their Reference 4), *may have inverted ventricles for the situs*, but not "by definition." For this reason we have proposed a logical sequence of analytical steps in such complex specimens: (1) diagnosis of the situs; (2) diagnosis of the direction of the apex; (3) diagnosis of the truncoconal morphology (crossed arteries, transposed arteries or single trunk); (4) diagnosis of the position of the ventricles; and (5) diagnosis of the associated defects.[2,3]

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3. **Anselmi G, Munoz S, Blanco P, et al:** Systematization and clinical study of dextroversion, mirror-image dextrocardia and laevoversion. Br Heart J 34:1085–1098, 1972

REPLY

We are fully aware that an atrial septal defect permits survival in transposition of the great arteries, as well as in isolated ventricular inversion. We meant to point out that this patient survived to age 9 years in spite of the presence of a complete